CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-061/SE2-007

21-062/SE2-008

ADMINISTRATIVE DOCUMENTS

NDA 21-061/SE2-007
December 21, 2000 Submission

PATENT INFORMATION

1) Patent No./Expiration: U.S. Patent 4,980,470; expires December 25, 2007

Type of Patent: Drug Substance

Patent Owner: Kyorin Pharmaceutical Co., Ltd.

2) Patent No./Expiration: U.S. Patent 5,880,283; expires December 5, 2015

Type of Patent: Drug Substance

Patent Owner: Kyorin Pharmaceutical Co., Ltd.

Bristol-Myers Squibb Co. is the exclusive licensee of U.S. Patents 4,980,470 and 5,880,283.

DECLARATION

The undersigned declares that U.S. Patents 4,970,470 and 5,880,283 cover the drug substance which is the subject of the present Supplemental New Drug Application.

David M. Morse
Signature of Authorized Person

DAVID M. MORSE
Name of Authorized Person

PATENT COUNSEL
Title of Authorized Person

December 11, 2000
Date

EXCLUSIVITY SUMMARY for NDA # 21-061 SUPPL # 007

Trade Name Tequin Tablets, 200 and 400 mg

Generic Name gatifloxacin HCl

Applicant Name Bristol-Myers Squibb Company HFD- 590

Approval Date October 12, 2001

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/___/ **NO / X /**

   b) Is it an effectiveness supplement? **YES/ X /** NO/___/

      If yes, what type (SE1, SE2, etc.)? **SE2**

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES / X / NO /___/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   d) Did the applicant request exclusivity?

      YES /___/NO / X /

      If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

      _____

      _____

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No – Please indicate as such).

YES /___/ NO / X /

If yes, NDA #_____Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO / X /

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety(including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES / X / NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 21-061
NDA # 21-062
NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #
NDA #
NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES / X / NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

   For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES / X / NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ **NO / X /**

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ **NO / X /**

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ **NO / X /**

If yes, explain:_____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1: **Study # AI420-064**
Investigation #2: **Study # AI420-065**
Investigation #3: Study #

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

   (a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

   Investigation #1 YES /___/ **NO / X /**

   Investigation #2 YES /___/ **NO / X /**

   Investigation #3 YES /___/ NO /___/

   If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # Study #

NDA # Study #

NDA # Study #

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ **NO / X /**
Investigation #2 YES /___/ **NO / X /**
Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # Study #

NDA # Study #

NDA # Study #

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #: **Study # AI420-064**
Investigation #: **Study # AI420-065**
Investigation #: Study #

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

[redacted] YES / X / NO /___/ Explain:

Investigation #2

[redacted] YES / X / NO /___/ Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____

_____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

_____

_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ **NO / X /**

If yes, explain: _____

_____ _____

Signature of Preparer Date

Title: Regulatory Health Project Manager

_____ _____

Signature of Acting Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Diana Willard
10/15/01 10:59:52 AM

Renata Albrecht
10/24/01 06:14:46 PM

EXCLUSIVITY SUMMARY for NDA # 21-062 SUPPL # 008

Trade Name Tequin Injection

Generic Name gatifloxacin HCl

Applicant Name Bristol-Myers Squibb Company HFD- 590

Approval Date October 12, 2001

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/___/ **NO / X /**

   b) Is it an effectiveness supplement? **YES/ X /** NO/___/

      If yes, what type (SE1, SE2, etc.)? **SE2**

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES / X / NO /___/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   d) Did the applicant request exclusivity?

      YES /___/NO **/ X /**

      If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

      _____

      _____

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No – Please indicate as such).

YES /___/ **NO / X /**

If yes, NDA #_____Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ **NO / X /**

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety(including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES / X / NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 21-061
NDA # 21-062
NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #
NDA #
NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

   YES / X / NO /___/
   skip to 3(a)

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain:_____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1: Study #
Investigation #2: Study #
Investigation #3: Study #

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

   (a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

   Investigation #1 YES /___/ **NO / X /**

   Investigation #2 YES /___/ **NO / X /**

   Investigation #3 YES /___/ NO /___/

   If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

   NDA # Study #

   NDA # Study #

   NDA # Study #

   (b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

   Investigation #1 YES /___/ **NO / X /**
   Investigation #2 YES /___/ **NO / X /**
   Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # Study #

NDA # Study #

NDA # Study #

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #: **Study # AI420-064**
Investigation #: **Study # AI420-065**
Investigation #: Study #

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

[redacted] YES / X / NO /___/ Explain:

Investigation #2

[redacted] YES/ X / NO /___/ Explain:

(a) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____

_____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

_____

_____

(b) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ **NO / X /**

If yes, explain: _____

_____ _____

Signature of Preparer Date

Title: Regulatory Health Project Manager

_____ _____

Signature of Acting Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Diana Willard
10/15/01 11:02:09 AM

Renata Albrecht
10/24/01 06:52:53 PM

FDA Links Searches Check Lists Tracking Link Calendars Reports Help

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)

View as Word Document

NDA Number:	021061	**Trade Name:**	TEQUIN
Supplement Number:	007	**Generic Name:**	GATIFLOXACIN
Supplement Type:	SE2	**Dosage Form:**	TABLETS
Regulatory Action:	OP	**COMIS Indication:**	TREATMENT OF BACTERIAL INFECTIONS
Action Date:	12/21/00		

Indication # 1 5 day treatment of acute exacerbation of chronic bronchitis

Label Adequacy: Does Not Apply

Formulation Needed: NO NEW FORMULATION is needed

Comments (if any): the study requirement for this indication is waived for this application as this indication is not applicable in the pediatric population

Ranges for This Indication

Lower Range	Upper Range	Status	Date
18 years	Adult	Waived	

This page was last edited on 10/9/01

/S/ Oct. 16, 2001

Signature Date

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)

View as Word Document

NDA Number:	021062	**Trade Name:**	TEQUIN
Supplement Number:	008	**Generic Name:**	GATIFLOXACIN
Supplement Type:	SE2	**Dosage Form:**	For Injection
Regulatory Action:	OP	**COMIS Indication:**	TREATMENT OF BACTERIAL INFECTIONS
Action Date:	1/3/01		

Indication # 1 5 day treatment of acute exacerbation of chronic bronchitis

Label Adequacy: Does Not Apply

Formulation Needed: NO NEW FORMULATION is needed

Comments (if any): the study requirement for this indication is waived for this application as this indication is not applicable in the pediatric population

Ranges for This Indication

Lower Range	Upper Range	Status	Date
18 years	Adult	Waived	

This page was last edited on 10/9/01

TSI

Signature

Oct. 16, 2001

Date

NDA 21-061 | SE2-007
December 21, 2000 submission

CERTIFICATION: DEBARRED PERSONS

Bristol-Myers Squibb Company hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug and Cosmetic Act in connection with this Application for TEQUIN™ (gatifloxacin) Tablets.

Robert Kessler

12/13/00

Date

Robert Kessler, Ph.D.
Director, Regulatory Science
Bristol-Myers Squibb Company
5 Research Parkway
P.O. Box 5100
Wallingford, CT 06447-7660
(203) 677-6163

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators

AI420-065 (Table B, Supplemental, 10-May-01)
AI420-065 (Table C, Amended 10-May-01)
AI420-065 (Status of Outstanding disclosures, 10-May-01)

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME: Deborah Derhergh, M.D.	Executive Director, Infectious Diseases Clinical Research
FIRM/ORGANIZATION: Bristol-Myers Squibb Company	
SIGNATURE: Deborah Derhergh	DATE: 10 May 2001

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators
AI420-064 (Table B, Supplemental, 10-May-01)
AI420-064 (Table C, Amended 10-May-01)
AI420-064 (Status of Outstanding disclosures, 10-May-01)

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	
Deborah Derhertogh, M.D.	Executive Director Infectious Diseases Clinical Research
FIRM/ORGANIZATION	
Bristol-Myers Squibb Company	
SIGNATURE	DATE
Deborah Derhertogh	10 May 2001

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

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FORM FDA 3454 (3/99)

Filing Meeting

Date of Meeting: February 7, 2001

NDA Numbers: NDA 20-061/SE2-007
NDA 20-062/SE2-008

Drug Names: Tequin (gatifloxacin) Tablets (NDA 21-061)
Tequin (gatifloxacin) Injection (NDA 21-062)

Proposed Indication: 5 Day Treatment of Acute Exacerbation of Chronic Bronchitis

Sponsor: Bristol-Meyers Squibb Company

Therapeutic Classification: Fluoroquinolone

Dates of Applications: December 21, 2000 (NDA 21-061/SE2-007)
January 2, 2001 (NDA 21-062/SE2-008)

Dates of Receipt: December 21, 2000 (NDA 21-061/SE2-007)
January 3, 2001 (NDA 21-062/SE2-008)

10 Month User Fee Goal Dates: October 21, 2001 (NDA 21-061/SE2-007)
November 3, 2001 (NDA 21-062/SE2-008)

12 Month Use Fee Goal Dates: December 21, 2001 (NDA 21-061/SE2-007)
January 3, 2002 (NDA 21-062/SE2-008)

User Fee Status: NDA 21-061/SE2-007: User Fee ID No. 3997
Paid

NDA 21-062/SE2-008: the data were incorporated by reference from NDA 21-0612/SE2-007

Submission Complete As Required Under 21 CFR 314.50? No (See Regulatory Requirements)

Patent Information Included? Yes

Exclusivity Requested? No

Debarment Statement Included? Yes

Financial Disclosure Information Included? Yes, but incomplete

Attendees:

Renata Albrecht, M.D.	Deputy Division Director, HFD-590
Rigoberto Roca, M.D.	Team Leader/Medical Officer, HFD-590
Marc Cavaille-Coll, M.D., Ph.D.	Team Leader/Medical Officer, HFD-590
Joyce Korvick, M.D.	Medical Officer, HFD-590
Rosemary Johann-Liang, M.D.	Medical Officer, HFD-590
Shukal Bala, Ph.D.	Team Leader/Microbiology, HFD-590
Peter Dionne, M.S.	Microbiologist, HFD-590
Karen Higgins, Sc.D.	Team Leader/Statistics, HFD-725
Kenneth Hastings, Ph.D.	Team Leader/Pharmacology, HFD-590
Steve Hundley, Ph.D.	Pharmacologist, HFD-590
Esther Putnam, Ph.D.	Pharmacology/Toxicology Assessor, RIVM, The Netherlands
Philip Colangelo, Ph.D.	Clinical Pharmacology & Biopharmaceutics, HFD-880
Antoine El-Hage, Ph.D.	Supervisory Pharmacologist, HFD-45
Ellen Frank, R.Ph.	Chief, Project Management Staff, HFD-590
Diana Willard	Regulatory Health Project Manager, HFD-590

Background

Bristol-Meyers Squibb Company (BMS) submitted two supplemental NDAs under section 505 (b)(1) of the Federal Food, Drug, and Cosmetic Act in support of a proposed 5-day treatment with Tequin of acute exacerbation of chronic bronchitis (AECB). Tequin is currently approved for a 7-to 10-day treatment regimen of AECB.

Medical – Dr. Johann-Liang

In support of a change from the currently approved 7- to 10-day Tequin treatment of AECB to a 5-day regimen, BMS submitted results from two clinical trials, AI420-064 and AI420-065, that enrolled a total of 828 patients. In addition, a study report from [redacted] for a 5-day study with Tequin of AECB that was conducted without any involvement on the part of BMS was submitted. This report from [redacted] is being submitted for informational purposes only.

Dr. Johann-Liang noted that, as discussed during a December 8, 2000 teleconference between BMS and the Division, investigator sites 23 and 24 in Study AI420-064 are under investigation by the FDA Division of Scientific Investigation (DSI). Of the 50 investigator sites in Study AI420-064, 37% of the patients enrolled in this study were from sites 23 and 24. BMS included data from these two sites in their submitted analysis but have conducted an analysis without the data from these two sites. The analysis of the data excluding sites 23 and 24 has not been submitted for review.

Dr. Johann-Liang provided the following chart for Study AI420-064:

	Sites 23 and 24 only	50 sites all together	%
No. of patients	193	582	37
No. of "Evaluable" organisms	96	238	40
No. of Evaluable organisms by breakdown of micro			
S. pneumo	17	41	41
S. aureus	30	68	44
M. catarralis	11	43	26
H. flu	22	55	40
H. paraflu	16	31	52
No. of Evaluable organisms by treatment arms			
Gatiflox 5 d	27	78	35
Gatiflox 7 d	29	78	37
Clarithro 10 d	40	82	49

From the medical Officers' perspective, these supplemental applications are fileable.

Statistical – Dr. Silliman

Dr. Higgins stated that Dr. Nancy Silliman will be the statistical reviewer for these supplemental NDAs.

Dr. Silliman has conducted a preliminary review of these supplements. She believes that even without the data from sites 23 and 24, Study AI420-064 supports the safety and efficacy of Tequin for 5-day treatment of AECB.

There are no statistical issues that would preclude filing of these supplemental applications.

Microbiology – Mr. Dionne

Mr. Dionne stated that sufficient numbers of isolates were submitted for evaluation. He noted that *Streptococcus pneumoniae* was eradicated with the 5-day Tequin regimen.

Dr. Cavaille-Coll suggested that the microbiology data be reviewed excluding the data from sites 23 and 24 in Study AI420-064.

These supplemental applications are fileable from the microbiologists' perspective.

Clinical Pharmacology and Biopharmaceutics – Dr. Colangelo

Dr. Colangelo stated that these supplemental NDAs contain no pharmacokinetic data.

Dr. Colangelo noted that the How Supplied section of the current label provides for a 7-day Tek-Pak. Ms. Willard will confer with the chemist for these applications, Dr. Smith, regarding whether BMS plans to provide for a 5-day Tek-Pak.

These supplemental applications are fileable from the clinical pharmacology and biopharmaceutics perspective.

Pharmacology –Dr. Hundley

From the pharmacologists' perspectives, these supplemental NDAs are fileable.

Chemistry – Dr. Smith

Ms. Willard conveyed a message from Dr. Smith that there are no chemistry issues that would prevent filing of these supplemental applications.

Division of Scientific Investigations – Dr. El-Hage

Dr. El-Hage strongly recommended that the Division not accept any data from sites 23 and 24 in Study AI420-064 without third party verification. DSI believes that unless BMS can provide the Agency with positive identification of each subject, the data from these two sites should be excluded from any analyses used as a basis of action for these supplemental applications.

Dr. Albrecht indicated that BMS should be made aware of the Division's level of discomfort with accepting data from these two investigator sites. As BMS has stated that an analysis has been conducted excluding the data from these two sites, this analysis should be submitted.

Regulatory requirement/Organization – On its face, these applications include a complete Form FDA 356h, DMF authorization, patent information, and debarment certification as required under 21 CFR 314.50.

The required financial disclosure information is not complete for these supplemental applications. The submission notes that only 128 out of 153 subinvestigators in Study AI420-064 have provided the required financial disclosure statements. For Study AI420-065, BMS states that 101 out of 118 subinvestigators in Study AI420-064 have provided the required financial disclosure statements (although the table provided by BMS indicates that financial disclosure statements are missing for 18, not 17, subinvestigators in Study AI420-065). Ms. Willard spoke with Dr. Robert Kessler of BMS on February 6, 2001 to discuss the missing financial disclosure statements. Although current Center policy is to file applications when financial disclosure information is incomplete, Dr. Kessler was informed of the requirement to have a complete financial disclosure record by the time an action is taken on these supplemental NDAs.

SAS transport files and case report forms were provided electronically for these supplemental NDAs.

Summary: It was agreed that these applications are acceptable for filing.

Ms. Willard will confer with Dr. Smith regarding plans by BMS to manufacture a 5-day Tek-Pak.

A facsimile transmission will be sent to BMS requesting submission of an analysis of the data, including tables and graphs, without the data from investigator sites 23 and 24 from Study AI420-064.

Minutes Preparer: _____
Diana Willard

Meeting Chair: _____
Renata Albrecht, M.D.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Diana Willard
3/14/01 08:45:34 AM

Renata Albrecht
4/24/01 12:11:09 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	
AI420-064 (Table A)	
AI420-064 (Table B)	
AI420-064 (Table C)	

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Roger M. Echols, M.D.	Vice President Infectious Diseases Clinical Research
FIRM/ORGANIZATION: Bristol-Myers Squibb Company	
SIGNATURE: for Roger Echols	DATE: 14 Dec 2000

Paperwork Reduction Act Statement

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Food and Drug Administration
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Rockville, MD 20857

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

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With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

(1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	AI420-065 (Table A)	
	AI420-065 (Table B)	
	AI420-065 (Table C)	

(2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

(3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Roger M. Echols, M.D.	Vice President Infectious Diseases Clinical Research
FIRM/ORGANIZATION	
Bristol-Myers Squibb Company	
SIGNATURE	DATE
for Roger Echols	14 Dec 2000

Paperwork Reduction Act Statement

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Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF FACSIMILE CORRESPONDENCE

DATE: August 27, 2001

TO: Joan Fung-Tumc

ADDRESS: Bristol-Meyers Squibb

TELEPHONE: 203-677-6370

FAX: 203-677-7867

FROM: Diana Willard

APPLICATIONS: NDA 21-061/S-007

SUBJECT: Environmental Assessment (EA) comments for NDA 21-061/S-007

Please refer to your December 21, 2000 submission for NDA 21-061/S-007 for Tequin. We have the following EA comments regarding this submission:

1. With respect to Section IV.D. of the July 1998 guidance entitled Environmental Assessment of Human Drug and Biologics Applications, please revise the EA (specifically for the water solubility, ionization constant, partition coefficient, and vapor pressure) so that the environmental assessment includes a description of the test method. The reference to the drug master file is not sufficient. The test method description should be sufficient for a reviewer to determine the scientific merit of the methodology. For example, the methodology used to determine water solubility should be identified, along with the temperature and pH at which the solubility was determined. If actual studies were not done (e.g., vapor pressure), please provide the basis for the statements.

2. The confidential appendices indicate that the acute toxicity results are on the active ingredient basis, however, it is not clear from the data provided in the summary table whether or not the acute toxicity studies are based on the active ingredient as opposed to the hydrate. Please clarify and update the appropriate sections in the EA to reflect this calculation.

3. On page 3 of the EA, you make the following statement: "Portions of the environmental assessment, including the appendices, are considered confidential by Bristol-Meyers Squibb Company, and should not be released under the Freedom of Information (FOI) Act. A separate, non-confidential report releasable under FOI is also provided". However, it is not clear what parts of the submitted EA are confidential and non-confidential. Please clearly identify the parts of the EA you consider non-confidential when submitting the revised EA.

If you have any additional questions you can contact Melissa Maust at (301) 594-5609 or you can contact me at (301) 827-2127.

Diana Willard
Regulatory Health Project Manager
Division of Special Pathogen and
Immunologic Drug Products

NDA 21-061/S-007
August 27, 2001

cc: HFD-590/NSchmuff
HFD-590/GHolbert
HFD-357/Mmaust
HFD-590/DWillard

DFS Keywords: admin memo; class quinolone

NOTE: This page not FAXED to sponsor.

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/s/

Jouhayna Saliba
8/27/01 12:53:14 PM
CSO
Jouhayna Saliba for Diana Willard

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF FACSIMILE CORRESPONDENCE

DATE: February 22, 2001

TO: Dr. Kessler

ADDRESS: Bristol-Meyers Squibb

TELEPHONE: 203-677-6163

FAX: 203-677-7867

FROM: Diana Willard

APPLICATIONS: NDA 21-061/S-007
NDA 21-062/S-008

SUBJECT: Reviewer Request

Please refer to your December 21, 2000 submission for NDA 21-061/S-007 and to your January 2, 2001 submission for NDA 21-062/S-008 for Tequin. We have the following request regarding these submissions:

As discussed during the December 8, 2000 teleconference between Bristol-Myers Squibb (BMS) and the Agency, it was agreed that it was acceptable to submit the Tequin supplemental NDAs for 5 day treatment of acute exacerbation of chronic bronchitis incorporating data from sites 23 and 24. BMS stated during this teleconference that an analysis has been conducted excluding patients from these two sites.

We have reviewed the independent auditors' report and find that we still have concerns regarding the authenticity of the patients from these sites. We therefore request that you submit the analysis that excluded patients from these two sites. All tables and graphs where the data from the two sites were incorporated should be updated and submitted to the supplemental NDAs.

If you have any questions, please contact me at (301) 827-2387.

Diana Willard
Regulatory Health Project Manager
Division of Special Pathogen and
Immunologic Drug Products

/s/

Diana Willard
2/22/01 07:38:22 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

MEMORANDUM OF FACSIMILE CORRESPONDENCE

DATE: February 9, 2001

TO: Dr. Kessler

ADDRESS: Bristol-Meyers Squibb

TELEPHONE: 203-677-6163

FAX: 203-677-7867

FROM: Diana Willard

APPLICATIONS: NDA 21-061/S-007
NDA 21-062/S-008

SUBJECT: Reviewer Requests/Comment

Please refer to your December 21, 2000 submission for NDA 21-061/S-007 and to your January 2, 2001 submission for NDA 21-062/S-008 for Tequin. We have the following requests/comment regarding these submissions:

1. If possible, please provide electronic study reports for Studies AI420-064 and AI420-065. Word documents would be acceptable. It is not necessary to provide the appendices electronically.

2. Please submit the relevant section/chapter of the Fleiss reference (Fleiss JL. Statistical Methods for Rates and Proportions, Second Edition, 1981. John Wiley and Sons, New York.) that is cited for adjusting the 95% confidence limits around the difference in response rates by steroid use/no steroid use.

3. The Fleiss method for calculating the CI is not in the original protocol for study AI420-064. Please clarify when this was added to the analysis plan.

If you have any questions, please contact me at (301) 827-2387.

Diana Willard
Regulatory Health Project Manager
Division of Special Pathogen and
Immunologic Drug Products

/s/

Diana Willard
2/9/01 12:43:53 PM
CSO

Minutes of a Teleconference

Meeting Date: March 20, 2001

Applications: NDA 21-061/S-007
Tequin (gatifloxacin HCl) Tablets

NDA 21-062/S-008
Tequin (gatifloxacin HCl)

Sponsor: Bristol- Myers Squibb Company

Subject: Investigator Sites 23 and 24 in Study AI420-064/Re-analyses

Attendees:

Bristol Myers Squibb:

Jeanne Breen, M.D.	Clinical
Michael Brown, Ph.D.	Statistics
Robert E. Kessler, Ph.D.	Director, Worldwide Regulatory Affairs
Karen Skuba, M.S.	Statistics

FDA:

Rosemary Johann-Liang, M.D.	Medical Officer, HFD-590
Rigoberto Roca, M.D.	Medical Team Leader, HFD-590
Diana Willard	Regulatory Health Project Manager, HFD-590

Background

Supplemental NDAs 21-061/S-007 and 20-062/S-008 were submitted on December 21, 2000 and January 3, 2001, respectively. These supplemental NDAs provide for a 5-day treatment with Tequin of acute exacerbation of chronic bronchitis (AECB). Tequin is currently approved for a 7 to 10-day treatment regimen of AECB.

As discussed during a December 8, 2000 teleconference between Bristol-Myers Squibb (BMS) and the Division, investigator sites 23 and 24 in Study AI420-064 are under investigation by the FDA Division of Scientific Investigation (DSI). Of the 50 investigator sites in Study AI420-064, 37% of the patients enrolled in this study were from sites 23 and 24. BMS included data from these two sites in their submitted analysis but have conducted an analysis without the data from these two sites. The analysis of the data excluding sites 23 and 24 has not been submitted for review.

Teleconference Objective

The objective of this teleconference was to discuss submission of an analysis and tables for Study AI420-064 excluding data from study sites 23 and 24.

Discussion

BMS stated that the analysis in the study report containing data from sites 23 and 24 for Study AI420-064 has been re-done excluding data from these 2 sites. In addition, the tables in the study report for Study AI420-064 have been re-constructed without data from these two sites. The appendices, however, have not been re-constructed without the data from these two sites. Dr. Johann-Liang stated that the tables in Volume 1, pages 49-84, and the tables in Volume 4 are the most critical to submit for her review.

Dr. Roca recommended that BMS submit an addendum to the supplemental NDAs with the re-done analysis. Included with this addendum should be BMS' conclusions regarding both efficacy and safety from the re-analysis. BMS should state that the re-analysis did/did not change the study conclusions and why/why not.

Regarding appendices, Dr. Roca recommended that BMS review the appendices and determine which ones they believe are critical to the review of the sNDAs. For example, if BMS determines that removal of sites 23 and 24 will change any conclusions, then the appendix(ces) that support that change in conclusions should be re-constructed and submitted without the data from sites 23 and 24.

BMS will make changes to the label proposed for the sNDAs and submit a revised proposed label.

Dr. Kessler predicted that submission of the requested material will take place by May 2001.

Summary

Submission of an analysis and tables for Study AI420-064 excluding data from study sites 23 and 24 was discussed. What to do about appendices containing data from these 2 sites was also discussed.

Minutes Preparer: _____
Diana Willard

Concurrence, Meeting Chair: _____
Rigoberto Roca, M.D.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Diana Willard
5/2/01 07:30:07 AM
CSO

Rigoberto Roca
5/8/01 11:12:15 AM
MEDICAL OFFICER

STATISTICAL REVIEW AND EVALUATION: 45 DAY MEETING REVIEW

NDA:	21-061 SE2-007
Name Of Drug:	Tequin (gatifloxacin) tablets
Applicant:	Bristol-Myers Squibb Pharmaceutical Research Institute
Submission Date:	December 21, 2000
Indication(s):	Acute Exacerbation of Chronic Bronchitis (AECB)
Number And Type Of Controlled Clinical Studies:	2 pivotal randomized, multicenter, double-blind, double-dummy, active-controlled studies (clarithromycin in study AI420-064; azithromycin in study AI420-065) 1 supportive study (study KF5501/03, conducted by [redacted])
Statistical Reviewer:	Nancy Silliman, Ph.D., SGE
Clinical Reviewer:	Joyce Korvick, MD, HFD-590
Project Manager:	Diana Willard, HFD-590

I. ORGANIZATION AND DATA PRESENTATION		YES	NO	N/A
A.	Is there a comprehensive table of contents with adequate indexing and pagination?	✓		
B.	Are the original protocols, protocol amendments and proposed label provided?	✓		
C.	Have the data been submitted electronically?	✓		
D.	If the data have been submitted electronically, has adequate documentation of the data sets been provided?	✓		

II. STATISTICAL METHODOLOGY

			YES	NO	N/A
A.	Are all primary efficacy studies of appropriate design to meet basic approvability requirements, within current Divisional policy statements or to the extent agreed upon previously with the sponsor by the Division?		✓		
B.	For each study, is there a comprehensive statistical summary of the efficacy analyses which covers the intent-to-treat population, evaluable subject population and other applicable sub populations (age, gender, race/ethnicity, etc.)?		✓		
1.	If subset analyses were not done, was an acceptable explanation of why given?				✓
C.	Based on the summary analyses of each study, do you believe:				
1.	The analyses are appropriate for the type data collected, the study design, and the study objectives (based on protocol and proposed label claims)?	✓			
2.	If there are multiple comparisons issues, has this been adequately addressed?		✓		
3.	Intent-to-treat (ITT and MITT) analyses are properly performed?	✓			
4.	Sufficient and appropriate references were included for novel statistical approaches?			✓	
D.	If interim analyses were performed, were they planned in the protocol and were appropriate significance level adjustments made?				✓
E.	Are there studies which are incomplete or ongoing?			✓	
F.	Is there a comprehensive, adequate analysis of safety data as recommended in the Clinical/Statistical Guideline?		✓		

III. FILEABILITY CONCLUSIONS

From a statistical perspective, this submission is considered reviewable with only minor further input from the sponsor.

Nancy Silliman, Ph.D.
Special Government Employee (SGE)

Concur: Karen Higgins, Sc.D.
Statistics Team Leader, DB III

cc:
Archival: NDA #21-061 SE2-007
HFD-590/Dr. Goldberger
HFD-590/Dr. Cavaille-Coll
HFD-590/Dr. Korvick
HFD-590/Ms. Willard
HFD-725/Dr. Huque
HFD-725/Dr. Higgins

/s/

Karen Higgins
2/14/01 10:17:44 AM
BIOMETRICS
For Nancy Silliman, SGE

Karen Higgins
2/14/01 10:18:49 AM
BIOMETRICS
45 Day checklist for Gatifloxacin AECB 5 days

7.1

USER FEE VALIDATION SHEET

NDA # 21-062 Supp. Type & # SLR-007 UFID #_____
(e.g., N000, SLR001, SE1001, etc.)

1. YES (NO) User Fee Cover Sheet Validated? MIS_Elements Screen Change(s):

2. YES (NO) APPLICATION CONTAINS CLINICAL DATA?
(Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

REF IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.

3. YES (NO) SMALL BUSINESS EXEMPTION

4. YES (NO) WAIVER GRANTED

5. YES (NO) NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other then bundling).
If YES, list all NDA #s, review division(s) and those for which an application fee applies.

NDA #	Division		
N_____	HFD-_____	Fee	No Fee
N_____	HFD-_____	Fee	No Fee

6. (YES) NO BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required
(Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N_____	HFD-_____	N_____	HFD-_____

7. P (S) PRIORITY or STANDARD APPLICATION?

/S/ 12/19/00
PM Signature / Date

/S/ 19Dec00
CPMS Concurrence Signature / Date

2/14/00

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Randall D. Curtiss
Bristol-Myers Squibb Company
P.O. Box 5400
Princeton, NJ 08543

2. TELEPHONE NUMBER *(Include Area Code)*

(609) 818-5220

3. PRODUCT NAME

Tequin TM (gatifloxacin) Tablets

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☑ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

3997

6. LICENSE NUMBER / NDA NUMBER

21-061

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☑ NO *(See reverse side if answered YES)*

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Robert E. Kessler, Ph.D., Director	Director Regulatory Science	21 Dec. 2000

FORM FDA 3397 (5/98)